IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Allen, Keith D.	Office action:	Qian, Celine X.
Serial No.:	09/816,790	Group Art Unit:	1636
Filed:	March 22, 2001	Docket No.:	R855/75658.023500
Title:	Transgenic Mice Containing Sulfotransferase Gene Disruptions		

DECLARATION OF JOHN BURKE PURSUANT TO 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, John E. Burke, residing at 16357 E. Berry Avenue, Centennial CO 80015, hereby declare:

1. I am currently, and have been since 1998, the Attorney of Record for the Applicant and Assignee, Deltagen, Inc. I am listed on the originally filed Power of Attorney for the present application. From December 1996 to December 1999, I was Of Counsel with the law firm of Pillsbury Madison & Sutro (currently Pillsbury Winthrop) where I represented Deltagen with respect to intellectual property matters, including patent matters relating to their transgenic mouse program. From December 1999 until December 2001, I served as Deltagen's Vice President of Intellectual Property, where I supervised Deltagen's internal patent department. All of the applications, including the present application, covering the 750 lines of mice in DeltaBase were drafted by Deltagen's patent department. From December 2001 until April 2003, I served as Deltagen's Senior Vice President and General Counsel. From April 2003 through April 2005, I was a partner with the Denver office of Merchant & Gould, where I continued to represent Deltagen with regard to intellectual matters, including patent matters. I am presently employed as a Shareholder with the Denver office of the law firm of Greenberg Traurig, where I am

responsible for prosecution of Deltagens's patent portfolio relating to their transgenic mice program, including the present application.

2. I am familiar with the present application. I am familiar with the Office Action mailed April 27, 2005. I am aware that the Examiner has rejected the claims, in part, for allegedly failing to meet the utility and enablement requirements. I am aware that the Examiner argues on page 10 of the Office Action that background and genetic factors have an effect on phenotypes.

3. I hereby declare that, as evidenced by the attached Exhibit, the subject matter of the present application, mSTp1 gene knockout mice, were compared with control mice of identical background.

4. I hereby declare that the claimed mSTp1 gene knockout mouse has been extensively analyzed using the tests set forth in the Examples. This data has been incorporated into Deltagen's commercial database product, DeltaBase. This database has been subscribed to by at least three of the world's largest pharmaceutical companies, Merck, Pfizer and GSK.

5. I hereby declare that I have accessed Deltagen's internal web-based DeltaBase database to review the data derived from analyses of the claimed mice. I hereby declare that the attached Exhibit contains three (3) pages, each representing a screen printout from DeltaBase. The first page is the Behavior Summary page summarizing changes relating to genotype associated with Gene 855, as prepared by Deltagen's pathology group. As noted at the top of the page, Gene 855 corresponds to the SULT1A1 sulfotransferase gene (which is an alternative name for the mSTp1 gene). As noted, the homozygous mice displayed significantly increased aggression towards their littermates, along with significant differences in the open field test (hyperactivity and less anxious than wild-type). The page further notes that for the behavioral tests, 9 homozygous mutant males were compared with 10 wild-type controls males. The page further describes how 129/OlaHsd x C57BL/6 F2N0 mice were produced. The table on the right side of the page provides the background of each of the homozygous (-/-) and wild-type control mice (+/+) used in the comparative tests. As is shown in the table, the mutant mice (-/-) and control mice (+/+)

are of identical F2N0 background (129/OlaHsd x C57BL/6). Specifically, the wild type control mice were the +/+ progeny of the intercrosses that generated the -/- mutant mice.

6. The second and third pages represent the "left" and "right" sides of a webpage showing the raw data derived from the open field tests for Gene 855 -/- mice. The gene number, 855, is indicated. As can be seen, each mouse was derived from the same ES cell line, 792 and each mouse is of identical background, F2N0. As can also be seen, each mouse tested is of approximately the same age and gender. The test dates are also indicated. All of the data corresponding to the F2N0 mice was entered prior to the filing date of the present application. The second and third pages also include the 1-p values resulting from comparison between the -/- mice and the control mice. The data derived were statistically significant (1-p values of 0.99 and 1).

7. In summary, the attached Exhibits show that the transgenic mice were compared with control mice of identical background. The phenotypes were based on a comparison with age, gender and strain matched control mice.

8. I further declare that all statements made herein of my own knowledge are true; and further that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the above-referenced application or any patent issuing thereon.

JER

John E. Burke, Reg. No. 35,836

8-11-05

Date

DeltaBase™ summaries data searching

gene | organ system | hot hits

Gene: 855 Name: Sult1a1 Family: Sulfotransferase Subfamily: Aryl Alternative Names

Nucleotide Sequence Accession: L02331 GI: 201069 External Links: Select External Database

Gene 855
Behavior

Changes related to genotype:

· Homozygous mutants showed increased aggression towards littermates.
· Homozygous mutants displayed an increase in total distance traveled in the Open Field Test.
· Homozygous mutants spent significantly more time in the central region of the Open Field Test.

ES cells derived from the 129/OlaHsd mouse substrain were used to generate chimeric mice. F1 mice were generated by breeding with C57BL/6 females. F2 homozygous mutant mice were produced by intercrossing F1 heterozygous males and females.

Homozygous mutant and wild-type control mice were evaluated for phenotypic changes by testing on five behavioral tasks: Open field test, Tail suspension test, Rotarod test, Hot plate test, and Metrazol test.

Mouse ID numbers are as follows:

9 homozygous mutant males (36649, 36668, 36669, 36676, 37649, 37652, 49591, 54671, 57940)
10 wild-type control males (36648, 36650, 36674, 36677, 37591, 37592, 37651, 43853, 43851, 43847)

Behavior Findings:

During home cage observations, homozygous mutant mice showed increased aggression towards their littermates. These animals attacked their littermates, and had to be housed separately to prevent such attacks.

When compared to age- and gender-matched wild-type control mice, homozygous mutants were significantly different from wild-types in the Open Field Test (total distance traveled). Mutants were hyperactive, in that they moved about and explored the open field more than wild-types.

Additionally, homozygous mutant mice were significantly different from wild-types in the Open field test when measuring the percentage of time spent in the central region. Homozygous mutant mice spent a higher percentage of time in the central portion of the open field compared to wild-types, suggesting that they were less anxious.

There were no other genotype-related differences noted between mutant and wild-type control mice for any other parameters evaluated during behavior testing.

Mice							
#	Sex	Genotype	F Gen.	N Gen.	Age	Validity	Release
36649	Male	-/-	2	0	74	V	T
36649	Male	-/-	2	0	82	V	T
36668	Male	-/-	2	0	73	V	T
36668	Male	-/-	2	0	78	V	T
36669	Male	-/-	2	0	73	V	T
36669	Male	-/-	2	0	78	V	T
36676	Male	-/-	2	0	71	V	T
36676	Male	-/-	2	0	76	V	T
37649	Male	-/-	2	0	73	V	T
37649	Male	-/-	2	0	79	V	T
37652	Male	-/-	2	0	73	V	T
37652	Male	-/-	2	0	79	V	T
49591	Male	-/-	2	0	76	V	T
49591	Male	-/-	2	0	81	V	T
54671	Male	-/-	2	0	75	V	T
54671	Male	-/-	2	0	84	V	T
57940	Male	-/-	2	0	70	V	T
57940	Male	-/-	2	0	78	V	T
36648	Male	+/+	2	0	74	V	T
36648	Male	+/+	2	0	82	V	T
36650	Male	+/+	2	0	74	V	T
36650	Male	+/+	2	0	82	V	T
36674	Male	+/+	2	0	71	V	T
36674	Male	+/+	2	0	76	V	T
36677	Male	+/+	2	0	71	V	T
36677	Male	+/+	2	0	76	V	T
37591	Male	+/+	2	0	71	V	T
37591	Male	+/+	2	0	77	V	T
37592	Male	+/+	2	0	71	V	T
37592	Male	+/+	2	0	77	V	T
37651	Male	+/+	2	0	73	V	T
37651	Male	+/+	2	0	79	V	T
43847	Male	+/+	2	0	72	V	T
43847	Male	+/+	2	0	84	V	T
43851	Male	+/+	2	0	72	V	T
43851	Male	+/+	2	0	84	V	T
43853	Male	+/+	2	0	72	V	T

(2)

Phenotypic Data - Open Field - - Microsoft Internet Explorer provided by Greenberg Traurig

Address https://deltaweb.deltagen.com/deltabase_web/DgenMetaAsp/W

View: View/Sort | Filter: Find • Find All | Related Data: <shift> or <ctrl> click to select row

Open Field | -- Select Filter -- | -- Select Screen --

Phenotypic Data - Open Field

(Highlight outliers when: wt control foldChange value < 0.6667 Or 1.5 < value) 9 Records 1 Page 250 records/page

F #	Age at Test (days)	Mouse	fecal boli	average velocity	total distance traveled (cm)	session time in central (%)	central zone entries	ambulatory episodes	Test Validity	Test Release Flag	Test Date	Test Id	Scientist
Gene: 855 Sulfotransferase (Aryl) - Sult1a1 (Accession) ES Cell Line: 792													
N#: 0 Genotype: -/- Gender: Male													
2	74	36649	6	25.81	383.45	11.06	58	21	V	T	2/21/2000	520287	Sara Siebel
2	73	36668	4	39.26	693.79	45.44	133	58	V	T	2/25/2000	520335	Todd Westerg
2	73	36669	10	25.93	437.41	32.21	74	12	V	T	2/25/2000	520359	Todd Westerg
2	71	36676	0	75.38	628.18	75.9	129	40	V	T	2/25/2000	520407	Todd Westerg
2	73	37649	5	75.73	335.56	85.29	76	22	V	T	3/3/2000	520746	Todd Westerg
2	73	37652	6	39.93	659.41	72.4	71	46	V	T	3/3/2000	520794	Todd Westerg
2	76	49591	1	24.31	726.48	51.32	93	67	V	T	5/5/2000 9:10:11 AM	553705	Todd Westerg
2	75	54671	4	49.01	1003.44	51.74	140	83	V	T	5/23/2000 9:10:24 AM	639095	Todd Westerg
2	70	57940	5	19.45	327.19	48.78	102	64	V	T	5/16/2000 8:57:27 AM	1851566	Heather Kell
				Average	632.77	52.68							
				Std. Dev.	217.11	22.95							
				WT Control Average (10)	324.19	20.86							
				WT Control Std. Dev.	207.69	16.24							
				1-p	0.99	1.							
				Fold Change	1.95	2.53							
				Relative Delta	1.49	1.96							

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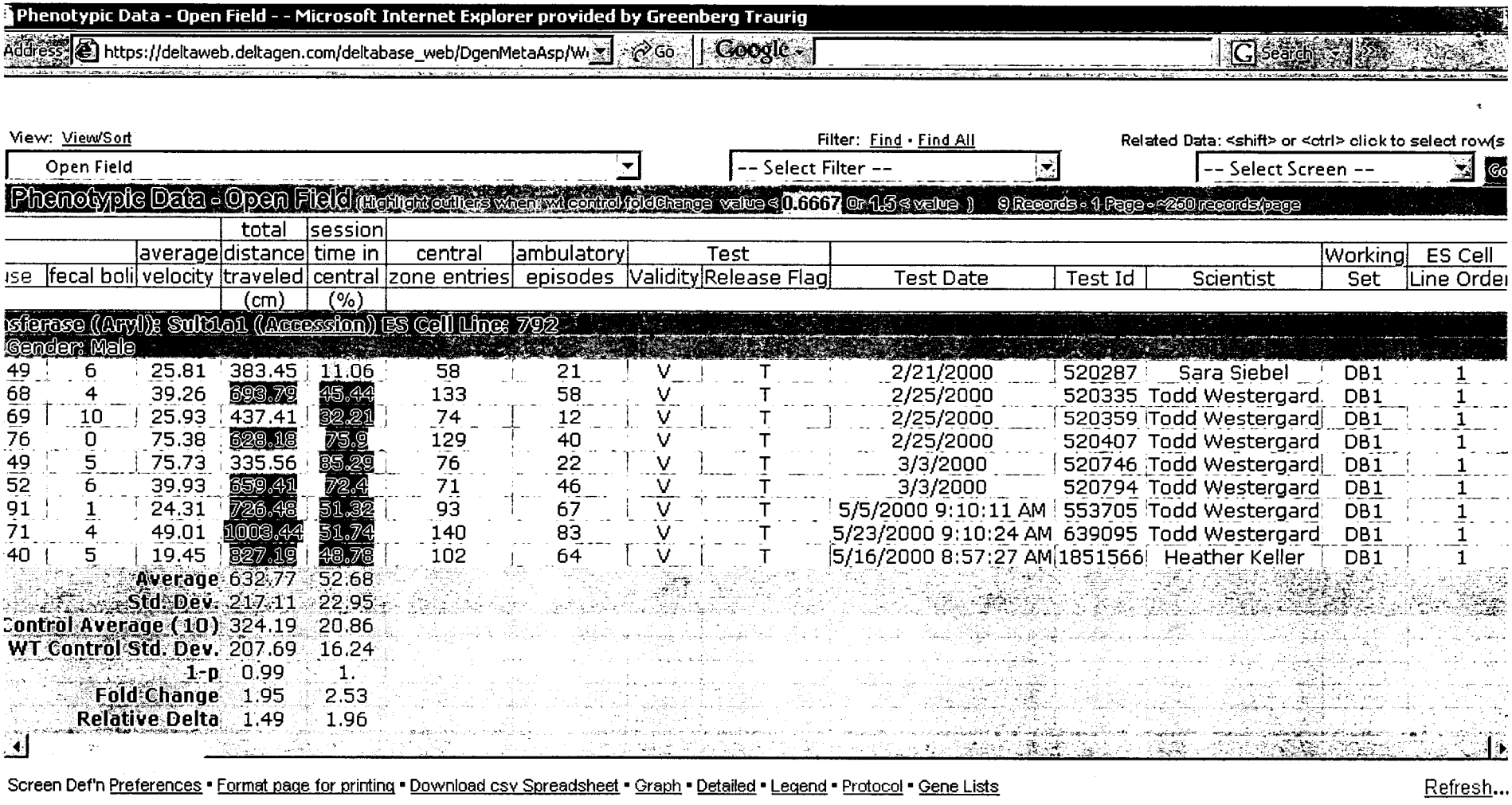
(2)



Phenotypic Data - Open Field - - Microsoft Internet Explorer provided by Greenberg Traurig

Address https://deltaweb.deltagen.com/deltabase_web/DgenMetaAsp/W

View: View/Sort — Open Field

Filter: Find • Find All — -- Select Filter --

Related Data: <shift> or <ctrl> click to select row(s — -- Select Screen --

Phenotypic Data - Open Field (Highlight outliers when: wt control foldChange value < 0.6667 Or 1.5 < value) 9 Records - 1 Page - <250 records/page

ise	fecal boli	average velocity	total distance traveled (cm)	session time in central (%)	central zone entries	ambulatory episodes	Test Validity	Test Release Flag	Test Date	Test Id	Scientist	Working Set	ES Cell Line Orde
sferase (Aryl): Sult1a1 (Accession) ES Cell Line: 792													
Gender: Male													
49	6	25.81	383.45	11.06	58	21	V	T	2/21/2000	520287	Sara Siebel	DB1	1
68	4	39.26	693.79	45.44	133	58	V	T	2/25/2000	520335	Todd Westergard	DB1	1
69	10	25.93	437.41	32.21	74	12	V	T	2/25/2000	520359	Todd Westergard	DB1	1
76	0	75.38	628.18	75.9	129	40	V	T	2/25/2000	520407	Todd Westergard	DB1	1
49	5	75.73	335.56	85.29	76	22	V	T	3/3/2000	520746	Todd Westergard	DB1	1
52	6	39.93	659.41	72.4	71	46	V	T	3/3/2000	520794	Todd Westergard	DB1	1
91	1	24.31	726.48	51.32	93	67	V	T	5/5/2000 9:10:11 AM	553705	Todd Westergard	DB1	1
71	4	49.01	1003.44	51.74	140	83	V	T	5/23/2000 9:10:24 AM	639095	Todd Westergard	DB1	1
40	5	19.45	327.19	48.78	102	64	V	T	5/16/2000 8:57:27 AM	1851566	Heather Keller	DB1	1
		Average	632.77	52.68									
		Std. Dev.	217.11	22.95									
		Control Average (10)	324.19	20.86									
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